REMARKS

In the Office Action mailed September 7, 2007, Claims 1, 2, 13-24, 29-33 and 38, 39, and 42-65 were pending for consideration. Claims 16-19 have been canceled while claims 44-65 remain withdrawn from consideration. All of the claims were objected to and/or rejected on various statutory grounds, each of which is addressed in turn below. By the present amendment, Claims 1, 32, and 33 have been amended. Specifically, Claims 1, 32, and 33 been amended to correct the misspelling of the term polyethyleneglycol, to replace the terms hydroxylpropyl methylcellulose derivative and glycerol monostearate with hydroxypropyl methyl cellulose phthalate, hydroxymethylcellulose succinate, ethyl cellulose, glycerol dipalmitate, and glycerol palmitostearate, and to include the limitation that the composition is formulated to release the drug over an extended period of time, said extended period of time being between 2 and 24 hours. Support for the amendment can be found in originally filed claim 19 as well as on page 3, paragraph [0038] of the published specification, and on page 5, paragraph [0063] and page 6 paragraph [0064]. Further, claims 32 and 33 have been amended to provide additional clarity with respect to the terms "caprylic acid more/diglycerides and mono- and diacetylated monoglycerides and "high molecular weight polysaccharide gums and resins." Support for the amendments can be found in the published application specification in paragraph [0063]. Applicants submit that no new matter has been added in the by the above described amendments.

It is to be understood that all amendments have been made solely for the purpose of expediting prosecution of the present application, and without conceding the correctness of the Examiner's rejection. Accordingly, Claims 1, 2, 13-15, 20-24, 29-33, 38-39, and 42-43 remain pending. Applicants respectfully submit that the present claims are allowable over the cited references, and that the rejections in view thereof are now moot.

Objections to claims

Claims 1, 32, and 33 have each been objected to for the misspelling of the term polyethyleneglycol. Each of the objected to claims has been amended to correct any misspelling of the term which existed. Applicants believe that such amendments are adequate to overcome the Examiner's objections

35 U.S.C. § 112 Rejections

First Paragraph

The Examiner has rejected claims 1-2, 13-24, and 29-33 under U.S.C § 112, first paragraph for allegedly failing to comply with the written description requirement with respect to the term "hydroxypropylmethylcellulose derivatives." As described above, the Applicants have amended Claims 1, 32, and 33 to replace the disputed terms with specifically enumerated hydroxypropylmethylcelluloses. Support for the claims is set forth above. Applicants assert that the present amendments to each of the rejected independent claims provides ample written description as required under 35 U.S.C. §112, first paragraph, and respectfully request that each of the rejections be withdrawn.

Second Paragraph

The Examiner has rejected claims 32-33 under 35 U.S.C. §112, second paragraph as allegedly being indefinite. Specifically, the Examiner rejected claim 1 for allegedly lacking clarity with respect to the phrase "caprylic acid mono/diglycerides and mono- and diacetylated monoglycerides" as well as for the use of the phrase "200-8000 MW". Applicants have amended claims 32-33 as described above in order to enhance the clarity of the claims. As such the

Applicants believe that each of the rejections by the Examiner under § 112, second paragraph should be withdrawn.

The Examiner has also rejected claims 1-2, 13-24, and 29-33 under 35 U.S.C. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Specifically, the Examiner has rejected the term "high" in the phrase "high molecular weight polysaccharide gum."

Applicants dispute that the presently pending claim are indefinite as the Examiner has asserted. However, in an effort to expedite prosecution of the pending application, Applicants have amended the rejected claims to eliminate the use of the phrase "high molecular weight polysaccharide gum" and replaced it with specifically exemplified species including acacia, xanthan gum, tragacanth, and shellac. Such an amendment is fully supported in the specification as described above. Applicants believe that the present amendment overcomes the Examiner's rejection.

35 U.S.C. § 102 Rejections:

The Examiner has rejected Claims 1, 13-15, 20-24, 29, 32-33, 38, and 42-43 under 35 U.S.C. § 102(b) as being allegedly anticipated by U.S. Pat. No. 5,891,469 (hereinafter "Amselem"). As shown above, each of the pending independent claims has been amended to include the limitation that the drug is released over an extended period of time of 2-24 hours. Such a limitation is not taught by Amselem. As such, Applicants respectfully submit that the cited reference does not teach each and every element of the pending clams, and therefore it is respectfully requested that this rejection be withdrawn.

35 U.S.C. § 103 Rejections

The Examiner has rejected Claims 1, 13-24, 29, 32-33, 38, and 42-43 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Amselem in view of The Merck Index (Eleventh Edition, Monograph 3924, 1989; pages 624-625), U.S. Patent No. 5,891,845 to Myers (hereinafter "Myers"), U.S. Patent No. 3,097,144 to Banker (hereinafter "Banker"). As Amselem and Myers are present in each of the combination rejections, Applicants response focuses on these two references.

Amselem teaches a solid dry coprecipitate of lipophilic active ingredients and tocopherol polyethyleneglycol succinate (TPGS) which is formed when the active ingredient is co-melted with the TPGS and at least one dispersion adjuvant (Col. 6, lines 23-27). The coprecipitate is made by co-melting the lipophilic active ingredient the TPGS and the dispersion adjuvant and then cooling the mixture to form a coprecipitate. The coporecipitates can be incorporated into oral dosage forms to provide improved release of the active agent in vitro and enhanced oral bioavailability. It is noteworthy that examples of the "at least dispersion adjuvant" which is required by Amselem include polyvinyl pyrrolidone (PVP), medium chain triglycerides or MCT oil, long chain triglycerides, and others. As stated by the Examiner, Amselem does not teach delivering active agent or drug over an extended period of time of from 2-24 hours. In fact, all of the release profiles taught by Amselem show immediate release of the active agents. See FIGS 1 & 2 and Col. 5, lines 55-57 ("After mixing with body fluids, such as gastric fluid, these compositions undergo quick dissolution with resultant micelle formulation or emulsification." (emphasis added))

The Examiner has attempted to overcome Amselem's failure to teach release over an extended period of time by combining it with Myers. Myers allegedly teaches "the advantages

of controlled release formulations to improve therapeutic value of the active drug component" teaches Vitamin E TPGS/drug compositions and related methods. In characterizing the prior art, Myers distinguishes itself by stating:

> These and other prior art cyclosporine emulsion or microemulsion compositions employ complex hydrophilic phase components, consisting of complex ethers, and lipophilic phase components, consisting of medium chain fatty acid trigylcerides, including neutral oils such as fractionated coconut oils. They also require surfactans, such as reaction products of vegitable oils and ethylene glycol, polyoxyethylene-sorbitan-fatty acid esters, ...polyvinyl pyrrolidones...The attempts to improve the emulsion and microemulsion formulations of [the prior art]...simply add more co-solvents and surfactants to what are already overly complex systems.

Col. 9, lines 3-16. Myers further states:

> The solid TPGS/drug composition of the present invention does not require the use of surfactants or non-evaporated co-solvents because the cyclosporine, or other drug component....

Col. 11, lines 3-5. Based on the statements in Myers, it is clear that Myers negatively characterizes and teaches away from using a dispersion adjuvant required by Amselem. Specifically, many of the compounds listed by Myers as being unnecessary and undesirable are listed in Amselem as the required dispersion adjuvant. Further, Myers states that "the new drug TPGS/drug delivery system of the present invention provides a slowly dissolving matrix that absorbs gastrointestinal fluid into the TPGS matrix at the dosage form/fluid interface, where a gel-like matrix crystal is formed." As set forth above, Amselem teaches that its formulation undergoes "quick dissolution" when in contact with gastric fluid. Col. 5, lines 55-57. Thus Myers actually distinguishes and teaches away from compositions of Amselem and other compositions which would include dispersion adjuvants or which dissolve quickly when placed in contact with gastric fluid.

As the Applicant has raised the issue of teaching away, the Applicant would like to review the current case law regarding teaching away for the Examiner's convenience. The Court of Appeals for the Federal Circuit has clearly stated that "an applicant may rebut a prima facie case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." In re Petersen, 315 F.3d 1325, 1331 (Fed. Cir. 2003). The Court has also stated that "[w]e have noted elsewhere, as a 'useful general rule,' that references that teach away cannot serve to create a prima facie case of obviousness." (emphasis added) McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1354 (Fed. Cir. 2001). In identifying the appropriate standard for teaching away, the Court has further stated:

> "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be **discouraged from following the path set out in the reference**, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, **a reference will teach away if it suggests** that the **line of development** flowing from the reference's disclosure **is unlikely to be productive** of the result sought by the applicant." (emphasis added) In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).

Clearly in the present case, a person of ordinary skill in the art would be discouraged from utilizing the teachings of Myers, which distinguishes and negatively characterizes the inclusion of the dispersion adjuvant compounds taught by Amselem to be required. Certainly, one skilled in the art would recognize the present combination of references as being contradictory to Myers teachings and thereby "unlikely to be productive of the result sought by the applicant."

Accordingly, the Applicant's respectfully submit that any the assert combinations of Amselem and Myers together is improper as Myers clearly teaches away from such a combination. Therefore, Applicants submit that the rejection of the present claims using

Amselem and Myers is improper and respectfully request that it be withdrawn and the claims be allowed.

The Examiner has also rejected claims 1-2, 16-24, 29, 32-33, 38-39, and 42-43 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 5,342,625 to Hauer et al (hereinafter "Hauer") in view of all or some of The Merck Index (Eleventh Edition, Monograph 2277, 3924; pages 624-625), Myers, U.S. Patent No. 6,458,373 to Lambert et al (hereinafter "Lambert") and Banker. As Hauer and Myers are present in each of the combination rejections, the Applicant response focuses on the incompatibility of these references.

Hauer teaches pharmaceutical compositions for delivering cyclosporine in microemulsion form having a hydrophilic phase, a lipophilic phase and a surfactant (Col. 6, lns. 45-53). The cyclosporine is found or carried in the lipophilic phase. As conceded by the Examiner in the office action (page 17, 1st paragraph), Hauer does not teach the release of the active agent over an extended period of time," (emphasis added) as required by the presently amended claims.

The secondary reference, Myers, relied upon by the Examiner to teach "the advantages of controlled release formulations to improve therapeutic value of the active drug component" teaches Vitamin E TPGS/drug compositions and related methods. The active agent in the compositions is said to be "dissolved directly into Vitamin E TPGS to form a true molecular solution—not an emulsion or micro-emulsion." (emphasis added) In characterizing the prior art, Myers states the following:

> "The emulsion and micro-emulsion cyclosporine formulations of the prior art suffer numerous disadvantages. They employ highly complex systems that provide generally immediate release formulation that disperse quickly in gastrointestinal tract, thereby permitting the amount of dissolved cyclosporine to be rapidly absorbed and taken into the blood stream at once." (Col. 8, lns. 44-50) (emphasis added)

In addition to the negative characterization of emulsion and micro-emulsion formulations and their numerous disadvantages, Myers specifically negatively characterizes and distinguishes Hauer as being "overly complex" and "seek[ing] to achieve immediate release and absorption of the drug." (Col. 8, ln. 56 to Col. ln. 16). Myers further states that Hauer's "[m]icroemulsions are dispersed quickly out of the emulsion into small particles that will be absorbed in the gut fairly quickly, if not instantly," (Col. 10, lines. 64-67)(emphasis added). Myers also distinguishes itself from Hauer and other emulsion and micro-emulsion formulations stating that "[t]he solid TPGS /drug composition of the present invention does not require the use of surfactants or non-evaporated co-solvents...In addition, the new drug TPGS/drug delivery system of the present invention provides a slowly dissolving matrix …" (Col. 11, lns.4-15) (emphasis added). In other words, Myers clearly distinguishes and teaches away from the compositions of Hauer and other emulsion and micro-emulsion formulations.

The Examiner is reminded of the teaching away standards set forth above. Clearly in the present case, a person of ordinary skill in the art would be discouraged from utilizing the teachings of Myers, which expressly references Hauer and other cyclosporine micro-emulsion formulations as "suffer[ing] numerous disadvantages," including being "overly complex," and releasing the drug "fairly quickly, if not instantly." Certainly, one skilled in the art would recognize the present combination of references as being contradictory to Myers teachings and thereby "unlikely to be productive of the result sought by the applicant."

Accordingly, the Applicant's respectfully submit that any the assert combinations of Hauer and Myers together is improper as Myers clearly teaches away from such a combination. Therefore, Applicants submit that the rejection of the present claims using Hauer and Myers is improper and respectfully request that it be withdrawn and the claims be allowed.

CONCLUSION

In view of the foregoing, the Applicants believe that Claims , 2, 13-15, 20-24, 29-33, 38-39, and 42-43 present allowable subject matter and the prompt allowance thereof is requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney, so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 28th day of February, 2008.

Respectfully submitted,

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